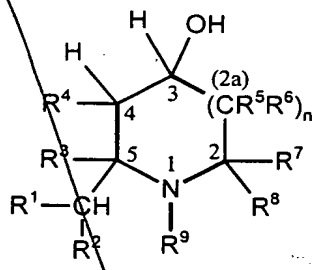
Claims

1. A process for the stereochemically controlled production of compounds of the general formula Ia',



Ia'

wherein the R^1R^2CH group in the 5-position of the cyclic parent structure and the hydroxy group in the 3-position of the cyclic parent structure are each in the trans position relative to each other and wherein the substituent R^4 in the 4-position and the hydroxy group in the 3-position of the cyclic parent structure are each in the cis position relative to each other, and wherein

n is 0 or 1,

R^1 is hydrogen; C_1-C_6-alkyl; or phenyl-C_1-C_6-alkyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, and

R^2 is hydrogen, or

R^1 and R^2 together are a double-bonded methylene group which may be substituted by C_1-C_5-alkyl or by phenyl-C_1-C_5-alkyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy,

R^3 is hydrogen, and

R^4 is hydrogen; lower alkyl; or phenyl-lower alkyl optionally substituted one or more times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, or

R^3 and R^4 also together are a C_2-alkylene chain; or a C_3-C_6-alkylene chain optionally containing 1 to 3 double bonds, which may be bridged by C_1-C_2-alkylene which is optionally substituted one or two times by lower alkyl,

R^5 is hydrogen; lower alkyl; hydroxy; lower alkoxy; phenyl-lower alkoxy or phenyl-lower alkyl each of which may be optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, and

R^6 is hydrogen, and

R^7 is hydrogen, and

R^8 is hydrogen; cyano: carboxy optionally esterified with cycloaliphatic or straight-chain or branched aliphatic C_1-C_6-alcohols containing optionally one to three double bonds, which are optionally substituted one to three times by halogen or lower alkoxy, or alternatively with phenyl-lower alcohols optionally substituted in the phenyl ring one to three times by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, carbonylamino optionally substituted at the nitrogen once by C_3-C_8-cycloalkyl lower alkanoyl or straight-chain or branched aliphatic C_1-C_6-alkanoyl, which in each case are optionally substituted one to three times by halogen or lower alkoxy, or by phenyl-lower alkanoyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, or at the nitrogen one or two times by C_3-C_8-cycloalkyl-lower alkyl or straight-chain or branched aliphatic C_1-C_6-alkyl, which in each case are optionally substituted one to three times by halogen or lower alkoxy, or by phenyl-lower alkyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, or also carbonylamino substituted at the nitrogen with a suitable amino protecting group; a monocyclic or bicyclic ring system with 3 to 10 ring carbon atoms which is optionally unsaturated one to four times, the ring carbon atoms of which may be replaced one to three times by nitrogen, oxygen and/or sulfur and which ring system may be substituted one to three times by lower alkyl, lower haloalkyl, lower alkoxy, hydroxy, halogen or by a lower alkylene chain which is bonded to two oxygen atoms bonded to adjacent carbon atoms of the ring system, or

may also stand for straight-chain or branched C_1-C_{12}-alkyl optionally containing one to three double bonds, which may optionally be substituted one to three times by halogen, hydroxy, lower alkoxy, carboxy optionally esterified with cycloaliphatic or straight-chain or branched aliphatic C_1-C_6-alcohols, which optionally contain one to three double bonds, and which are optionally substituted one to three times by halogen or lower alkoxy, or alternatively carboxy esterified with phenyl-lower alcohols optionally substituted in the phenyl ring one to three times by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy; cyano, mercapto, lower alkylthio, amino, lower alkylamino, carbonylamino optionally substituted once at the nitrogen by C_3-C_8-cycloalkyl-lower alkanoyl or straight-chain or branched aliphatic C_1-C_6-alkanoyl, which in each case are optionally substituted one to three times by

halogen or lower alkoxy, or by phenyl-lower alkanoyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, or carbonylamino substituted once or twice at the nitrogen by C_3-C_8-cycloalkyl-lower alkyl or straight-chain or branched aliphatic C_1-C_6-alkyl, which are each optionally substituted one to three times by halogen or lower alkoxy, or by phenyl-lower alkyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, or alternatively carbonylamino substituted at the nitrogen with a suitable amino protecting group, a monocyclic or bicyclic ring system with 3 to 10 ring carbon atoms which is optionally unsaturated one to four times, the ring carbon atoms of which may be replaced one to three times by nitrogen, oxygen and/or sulfur and which ring system may be substituted one to three times by lower alkyl, lower haloalkyl, lower alkoxy, hydroxy, halogen or by a lower alkylene chain which is bonded to two oxygen atoms bonded to adjacent carbon atoms of the ring system, or

R^5 and R^8 also, together with the carbon atoms to which they are bonded, may form a monocyclic or bicyclic ring system with 5 to 10 ring carbon atoms which optionally contains 1 to 3 double bonds, the carbon atoms of which which do not bear the substituents R^5 or R^8 may be replaced one to three times by sulfur, oxygen and/or nitrogen, and which optionally may be substituted one to three times by lower alkyl, lower haloalkyl, lower alkoxy, lower haloalkoxy, hydroxy, halogen or by a lower alkylene chain which is bonded to two oxygen atoms bonded to adjacent carbon atoms of the ring system, or

R^6 and R^7 also together may form a bond, and

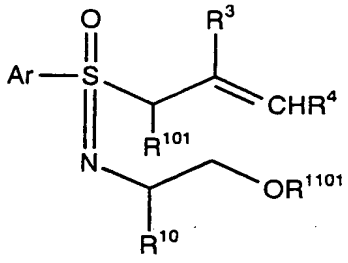
R^5 and R^8, together with the carbon atoms to which they are bonded, may form an aromatic C_6-ring system which may be fused with 2 to 4 further carbon atoms to form a bicyclic ring system having a total of 3 to 5 double bonds which contains a total of 8 to 10 ring carbon atoms, wherein the carbon atoms of this C_6- to C_{10}-ring system which do not bear the substituents R^5 or R^8 may be replaced one to three times by sulfur, oxygen and/or nitrogen, and wherein this C_6- to C_{10}-ring system may optionally be substituted one to three times by lower alkyl, lower haloalkyl, lower alkoxy, lower haloalkoxy, hydroxy, halogen or by a lower alkylene chain which is bonded to two oxygen atoms bonded to adjacent carbon atoms of the ring system,

R^9 is hydrogen; lower alkyl; phenyl-lower alkyl optionally substituted one to three times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy; or an amino protecting group, or

R^8 and R^9 also together may form a C_3-C_4-alkylene chain,

and their acid addition salts, wherein any reactive groups which may be present may be blocked in compounds of Formula Ia' by suitable protecting groups, characterized in that

a) a compound of the general formula II,

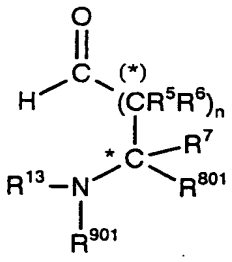


II

wherein R^3 and R^4 have the above meanings, R^{101} has the meaning given above for R^1 with the exception of an optionally substituted methylene group, Ar stands for phenyl optionally substituted one to three times by lower alkyl, R^{10} is lower alkyl, or phenyl optionally substituted once in the phenyl ring by lower alkyl or by hydroxy protected with a suitable protecting group, or phenyl-lower alkyl optionally substituted once in the phenyl ring by lower alkyl, and R^{1101} stands for a silyl protecting group, is reacted in succession with a base suitable for the deprotonation thereof, an organometallic reagent of the general formula VII,

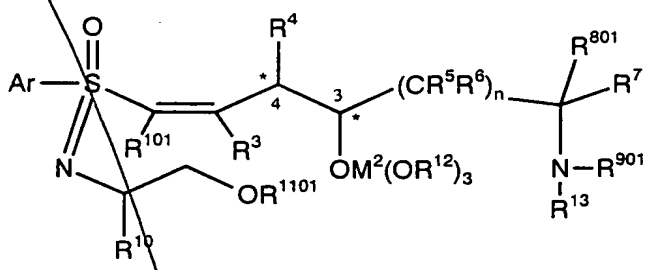
VII

wherein X stands for halogen, M^2 is a tetravalent transition metal and R^{12} stands for lower alkyl, phenyl or phenyl-lower alkyl, and a stereoisomer of a compound of the general formula VIII,



VIII

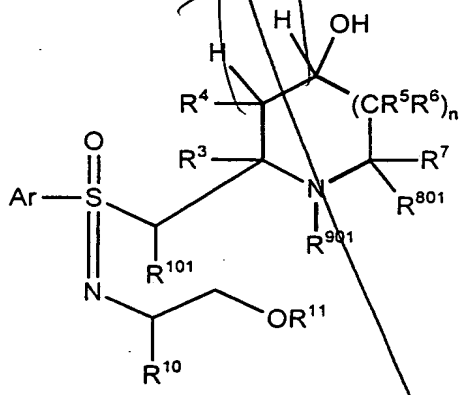
wherein R^5, R^6, R^7 and n have the above meanings, R^{801} has the meaning of R^8, with any reactive groups if necessary being blocked by base-stable protecting groups, R^{901} stands for hydrogen or together with R^{801} stands for a C_3-C_4-alkylene chain and R^{13} is an amino protecting group which when cleaved leaves behind a nitrogen nucleophile, to form a stereoisomer of a compound of the general formula IX,



IX

wherein R^{101}, R^3, R^4, R^5, R^6, R^7, R^{801}, R^{901}, R^{10}, R^{1101}, R^{12}, R^{13}, n, Ar and M^2 have the above meanings,

b) the resulting compound of Formula IX is converted, by treatment with a reagent suitable for removing the group R^{13}, into a compound of the general formula Xa,

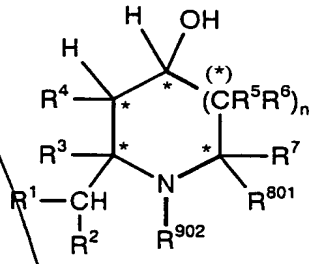


Xa

wherein R^{101}, R^3, R^4, R^5, R^6, R^7, R^{801}, R^{901}, R^{10}, n and Ar have the above meanings and R^{11} stands for hydrogen or a silyl protecting group and, if R^{901} stands for hydrogen, the nitrogen atom in the cyclic parent structure of the resulting

compound of Formula Xa is blocked with a base-stable protecting group and any silyl protecting group R^{11} which may still be present is cleaved off, and

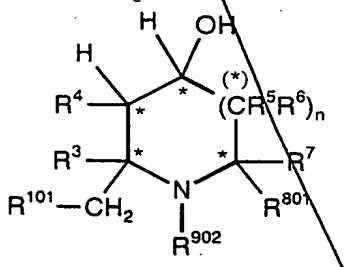
c) for the production of a compound of the general formula Ia,



Ia

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{801} and n have the above meanings and R^{902} stands for a base-stable protecting group or, together with R^{801}, for a C_3-C_4-alkylene chain,

ca) a resulting compound of Formula Xa or a compound produced by cleaving off the silyl protecting group R^{11} is reacted with a reagent suitable for the reductive cleavage of the sulfonimidoyl-alkyl bond, in order to obtain a compound of the general formula Ib,

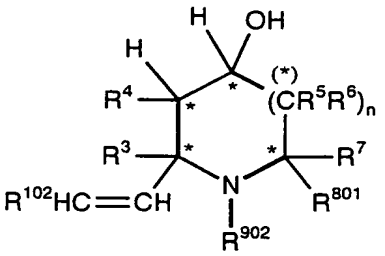


Ib

wherein R^{101}, R^3, R^4, R^5, R^6, R^7, R^{801}, R^{902} and n have the above meanings, or

cb) in a resulting compound of Formula Xa wherein R^{101} does not stand for hydrogen, the sulfonimidoyl-alkyl bond is cleaved after electrophilic activation of

the sulfonimidoyl unit under the conditions of a base-induced elimination, in order to obtain a compound of the general formula Ic,



Ic

wherein R^3, R^4, R^5, R^6, R^7, R^{801}, R^{902} and n have the above meanings and R^{102} stands for C_1-C_5-alkyl or for phenyl-lower alkyl optionally substituted one or more times in the phenyl ring by lower alkyl, lower haloalkyl, lower alkoxy or lower haloalkoxy, the lower alkylene chain of which phenyl-lower alkyl may contain 1 to 5 carbon atoms,

and if desired any protecting groups are cleaved again in compounds of Formula Ia and if desired the optionally released NH group in the 1-position of the cyclic parent structure is reacted with a reagent capable of N-alkylation or one capable of amide formation or is blocked with an amino protecting group, in order to obtain compounds of Formula Ia'.

2. A process according to Claim 1 for producing compounds of the general formula Ib and the compounds obtainable therefrom by cleaving any protecting groups which may be present and by reacting any free NH group in the 1-position of the cyclic parent structure with a reagent capable of N-alkylation or of amide formation or by blocking the above NH group which may be free with an amino protecting group, in accordance with Claim 1.

3. A process according to Claim 1, wherein a base-labile protecting group is used as the amino protecting group R^{13} in compounds of Formula VIII and wherein in process step b) a base is used as the reagent for removing the protecting group R^{13}.

4. A process according to Claim 3, wherein the base-labile protecting group is the fluoren-9-yl-methyloxy-carbonyl radical.

5. A process according to Claim 4, wherein piperidine is used as the base.

6. A process according to Claim 1, wherein toluene is used as solvent at least in process step a).

7. A process according to Claim 1, wherein samarium (II) iodide is used as reagent for the reductive cleavage of the sulfonimidoyl-alkyl bond in compounds of the general formula Xa in process step ca).

8. A process according to Claim 1, wherein R^4 is not hydrogen in each of the compounds of the general formulae Ia', Ia, Ib, Ic, II, IX and Xa.

9. A process according to Claim 1, wherein tert. butyl-dimethylsilyl or trimethylsilyl is used as the silyl protecting group R^{1101}.

10. A process according to Claim 1 for the production of compounds of the general formula Ia', wherein R^8 is hydrogen, lower alkyl, phenyl, phenyl-lower alkyl or lower-alkoxy lower alkyl, or R^6 and R^7 together form a bond and R^5 and R^8, together with the carbon atoms to which they are bonded, form an aromatic C_6-ring system or wherein R^8 together with R^9 forms a C_3-C_4-alkylene chain.

11. Compounds of the general formula Xa according to Claim 1,
and also compounds obtainable by removal of any protecting groups which may be present from compounds of Formula Xa and acid addition salts of free amines of Formula Xa, wherein in each case the sulfur-containing substituent in the 5-position and the hydroxy group in the 3-position of the cyclic parent structure are in the trans position relative to each other and wherein the substituent R^4 in the 4-position and the hydroxy group in the 3-position of the cyclic parent structure are each in the cis position relative to each other.

12. Compounds of the general formula Xa according to Claim 11 which contain a secondary nitrogen atom in the cyclic parent structure which is protected by the tert. butoxycarbonyl protecting group.

13. Compounds of the general formula Xa according to Claim 12, wherein R^{901} is hydrogen or together with R^{801} forms a C_3-C_4-alkylene chain.

14. The use of samarium (II) iodide for the reductive desulfurisation of alkyl-sulfonimidoyl compounds of the general formula Xa from Claim 1.

15. The use of (R_S)-4(S)-isopropyl-2-p-toluoyl-4,5-dihydro[1,2λ^6,3]oxathiazol-2-oxide, (S_S)-4(S)-isopropyl-2-p-toluoyl-4,5-dihydro[1,2λ^6,3]oxathiazol-2-oxide, (R_S)-4(R)-isopropyl-2-p-toluoyl-4,5-dihydro[1,2λ^6,3]oxathiazol-2-oxide and of (S_S)-4(R)-isopropyl-2-p-toluoyl-4,5-dihydro[1,2λ^6,3]-oxathiazol-2-oxide in processes for the stereochemically controlled production of azacyclic compounds according to Claim 1.

16. The use of [S_S,N(1S)]-N-[1-[[tert.-butyldimethylsilyl)oxy]methyl]-2-methylpropyl]-S-methyl-S-(4-methylphenyl)sulfoximide and of [R_S,N(1R)]-N-[1-[[tert.-butyldimethylsilyl)oxy]-methyl]-2-methylpropyl]-S-methyl-S-(4-methylphenyl)sulfoximide in processes for the stereochemically controlled production of azacyclic compounds according to Claim 1.